

Attorney Docket No.: **13257.00044 (UMD-0084)**
Inventors: **Sciorra and Zimnoch**
Serial No.: **09/869,741**
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This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (original): A method of separating at least one target substance from at least one non-target substance in a sample containing a mixture of substances, which comprises:

mixing the sample with a quantity of magnetic particles to produce a suspension comprising a magnetic component and a non-magnetic component, wherein the magnetic component comprises magnetic particles bound to the target substance through at least one moiety on the surface of the magnetic particles that directly or indirectly binds to the target substance, and the non-magnetic component comprises the remainder of the sample;

placing the suspension onto a substrate material;

exposing the substrate material containing the suspension to a magnetic field of sufficient strength to cause the magnetic component to migrate across the substrate material; and

repeatedly applying a pre-determined increase in the magnetic field in a pulsing manner with a frequency sufficient to cause the magnetic component to separate spatially from the non-magnetic component of the suspension.

Claim 2 (original): The method of claim 1 comprising the step of removing the magnetic component from the substrate material.

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Claim 3 (original): The method of claim 1 comprising the step of removing the magnetic particles from the target substance.

Claim 4 (original): The method of claim 1 wherein the magnetic particles have uniform physical and magnetic properties.

Claim 5 (original): The method of claim 1 wherein the magnetic particles are substantially identical.

Claim 6 (original): The method according to claim 1 wherein the magnetic particles are beads.

Claim 7 (original): The method according to claim 5 wherein the magnetic particles have a diameter from about 0.05 microns to about 4.5 microns.

Claim 8 (original): The method of claim 1 wherein the magnetic particles are chosen from the group consisting of ferromagnetic, paramagnetic or superparamagnetic particles.

Claim 9 (original): The method of claim 8 wherein the magnetic particles are superparamagnetic particles.

Claim 10 (original): The method of claim 1 wherein the magnetic particles include at least two different magnetic particles.

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Claim 11 (original): The method of claim 10 wherein the at least two different magnetic particles have different respective physical or electromagnetic properties.

Claim 12 (original): The method of claim 1 wherein the moieties on the surface of the magnetic particles are ligands that directly bind to the target substance.

Claim 13 (original): The method of claim 1 wherein the moieties on the surface of the magnetic particles are capture agents that bind to at least one ligand that binds to the target substance.

Claim 14 (original): The method of claim 12 or 13, wherein the ligand binds to more than one target substance.

Claim 15 (original): The method of claim 13, wherein the capture agent binds to more than one ligand.

Claim 16 (original): The method of claim 12 or 13, wherein the ligands are selected from the group consisting of monoclonal antibodies and polyclonal antibodies.

Claim 17 (original): The method of claim 1, wherein the sample comprises desired components and undesired components.

Claim 18 (original): The method of claim 17, wherein the desired components are biological materials selected from the

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group consisting of eucaryotic cells, procaryotic cells, subcellular organelles, viruses, proteins, peptides, nucleic acids, lipids, carbohydrates, and complex molecules comprising a combination of at least two of nucleic acids, proteins, lipids and carbohydrates.

Claim 19 (original): The method of claim 17, wherein the undesired components are biological materials selected from the group consisting of malignant cells, toxin-producing cells, bacteria, fungi, viruses, microbial parasites, proteins, peptides, and nucleic acids.

Claim 20 (original): The method of claim 17, wherein the desired component is a specific cell type and the undesired components comprise other cell types present in the sample.

Claim 21 (original): The method of claim 20, wherein the sample is derived from blood of a gestating female, and wherein the desired component comprises fetal cells disposed within the sample and the undesired component comprises maternal cells.

Claim 22 (original): The method of claim 17, wherein the target substance is the desired component, and the non-target substance is an undesired component of the sample.

Claim 23 (original): The method of claim 17, wherein the target substance is an undesired component of the sample, and the non-target substance is a desired component of the sample.

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Claim 24 (original): The method of claim 1 wherein the substrate material permits differential rates of migration between the magnetic component and the non-magnetic component.

Claim 25 (original): The method of claim 24, wherein the substrate material comprises a viscous solution that substantially prevents diffusion of the magnetic component unless a magnetic force is applied.

Claim 26 (original): The method of claim 25, wherein the substrate material is methylcellulose.

Claim 27 (original): The method of claim 26, comprising a solution of between about 1.7% and 2.0% methylcellulose.

Claim 28 (original): The method of claim 1 wherein the substrate material is a growth media for growing at least one substance contained in the mixture.

Claim 29 (original): The method of claim 1 wherein the coating step comprises placing the magnetic mixture along one edge of the substrate material.

Claim 30 (original): The method of claim 1 comprising the step of labeling the target substance with a fluorescent marker.

Claim 31 (original): The method of claim 1 comprising the step of labeling the non-target substance with a fluorescent marker.

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Claim 32 (original): The method of claim 1 wherein the magnetic field is of a strength of about 1.5 to about 2.0 Tesla.

Claim 33 (original): The method of claim 1 wherein the magnetic field is of a strength of at least 3.0 Tesla.

Claim 34 (original): The method of claim 1 wherein the frequency at which the magnetic field is activated and deactivated is from about 0.5 to about 10 seconds per pulse.

Claim 35 (original): The method of claim 1 wherein the frequency at which the magnetic field is activated and deactivated is from about 1.0 to about 2.0 seconds per pulse.

Claim 36 (original): The method of claim 1 wherein the frequency at which the magnetic field is activated and deactivated is about 2.0 seconds per pulse.

Claim 37 (original): The method of claim 1 wherein the magnetic field has a strength that varies substantially linearly with distance.

Claim 38 (original): The method of claim 36 wherein the magnetic field strength varies substantially linearly with distance within a plane of the substrate material.

Claim 39 (original): The method of claim 1 wherein the activating and deactivating of the magnetic field is performed at a frequency such that the pulses overlap in time.

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Claim 40 (original): An apparatus for separating at least one target substance from at least one non-target substance in a sample containing a mixture of substances comprising

a coil operating in conjunction with a power supply, wherein the coil produces variable pulsed magnetic fields;

a substrate that includes a magnetic mixture, the magnetic mixture comprising a magnetized form of a component capable of being transported across the surface of the substrate by the action of the pulsed magnetic fields; and

a sample chamber located within the coil, wherein the sample chamber is capable of receiving the substrate.

Claim 41 (original): The apparatus of claim 40, comprising a switching box operating in conjunction with the power supply and the coil.

Claim 42 (original): The apparatus of claim 41 comprising a capacitor bank operating in conjunction with the power supply, the coil, and the switching box.

Claim 43 (original): The apparatus of claim 42 wherein the switching box electrically isolates the capacitor bank from the coil.

Claim 44 (original): The apparatus of claim 43 wherein the switching box electrically connects in parallel the capacitor bank to the power supply.

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Claim 45 (original): The apparatus of claim 44 wherein the switching box electrically isolates the capacitor bank from the power supply.

Claim 46 (original): The apparatus of claim 45 wherein the switching box electrically connects in series the capacitor bank to the coil.

Claim 47 (original): The apparatus of claim 40 comprising a bank of capacitors charged by the power supply through a resistance circuit, wherein the resistance circuit comprises resistors wired in parallel.

Claim 48 (original): The apparatus of claim 47 wherein the bank of capacitors are wired in parallel.

Claim 49 (original): The apparatus of claim 40 wherein the coil is energized by a bank of capacitors wired in series.

Claim 50 (original): The apparatus of claim 41 wherein the switching box comprises manually actuated switches.

Claim 51 (original): The apparatus of claim 41 wherein the switching box comprises automated switches.

Claim 52 (original): The apparatus of claim 42 wherein the capacitor bank comprises at least six capacitors.

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Claim 53 (original): The apparatus of claim 42 wherein the capacitor bank comprises 12 capacitors.

Claim 54 (original): The apparatus of claim 40 wherein the coil comprises about 20,000 amp turns.

Claim 55 (original): The apparatus of claim 40 comprising permanent magnetic elements located within the coil.

Claim 56 (original): The apparatus of claim 56 wherein the permanent magnetic elements locally increase the strength of the magnetic field within the coil.

Claim 57 (original): The apparatus of claim 42 wherein the switching box, the power supply, the capacitor bank, and the coil are co-located.

Claim 58 (original): The apparatus of claim 40 comprising a bank of capacitors which discharge in series.

Claim 59 (original): The apparatus of claim 40 wherein the fields are of a strength of at least 0.7 Tesla.

Claim 60 (original): The apparatus of claim 40 wherein the magnetic field is of a strength of about 1.5 to about 2.0 Tesla.

Claim 61 (original): The apparatus of claim 40 wherein the magnetic field is of a strength of at least 3.0 Tesla.

Claim 62 (original): The apparatus of claim 40 wherein the fields vary at a period of about once every two minutes.

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Claim 63 (original): The apparatus of claim 40 wherein the period at which the magnetic field is activated and deactivated is from about 0.5 to about 10 seconds per pulse.

Claim 64 (original): The apparatus of claim 40 wherein the period at which the magnetic field is activated and deactivated is from about 1.0 to about 2.0 seconds per pulse.

Claim 65 (original): The apparatus of claim 40 wherein the period at which the magnetic field is activated and deactivated is about 2.0 seconds per pulse.

Claim 66 (original): The apparatus of claim 40 comprising a power source operably connected to the coil, wherein the power source continuously energizes the coil.

Claim 67 (original): An apparatus for separating at least one target substance from at least one non-target substance in a sample containing a mixture of substances comprising at least two coils, the at least two coils operating in conjunction with a power supply wherein the at least two coils produces variable pulsed magnetic fields.

Claim 68 (original): The apparatus of claim 67 wherein the at least two coils is a first coil and a second coil.

Claim 69 (original): The apparatus of claim 68 wherein the first coil contains more turns than the second coil.

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Claim 70 (original): The apparatus of claim 68 wherein the first coil contains about a factor of 6 more turns than the second coil.

Claim 71 (original): The apparatus of claim 68 comprising a sample chamber located within the second coil.

Claim 72 (original): The apparatus of claim 71 wherein the sample chamber is capable of receiving a substrate.

Claim 73 (original): The apparatus of claim 72 wherein the substrate includes a magnetic mixture, the magnetic mixture comprising a magnetized form of a component desired to be separated from the magnetic mixture.

Claim 74 (original): The apparatus of claim 67 comprising a switching device operating in conjunction with the power supply and the at least two coils.

Claim 75 (original): The apparatus of claim 74 comprising a capacitor bank operating in conjunction with the power supply, the at least two coils, and the switching device.

Claim 76 (original): The apparatus of claim 75 wherein the switching device electrically connects each capacitor in the capacitor bank separately to the at least two coils.

Claim 77 (original): The apparatus of claim 76 wherein each capacitor is electrically isolated from the power supply while electrically connected to the at least two coils.

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Claim 78 (original): The apparatus of claim 76 wherein the switching device electrically connects each capacitor in the capacitor bank sequentially to the at least two coils.

Claim 79 (original): The apparatus of claim 78 wherein a discharge pulse from a capacitor overlaps in time with a discharge pulse from the previously discharged capacitor.

Claim 80 (original): The apparatus of claim 75 wherein the switching device electrically connects each capacitor to the power supply when the capacitor is not electrically connected to the at least two coils.

Claim 81 (original): The apparatus of claim 75 wherein the switching device electrically isolates the capacitor bank from the power supply.

Claim 82 (original): The apparatus of claim 74 wherein the switching device is a rotating cam.

Claim 83 (original): The apparatus of claim 74 wherein the switching device is an electronic switch.

Claim 84 (original): The apparatus of claim 75 wherein the capacitor bank comprises at least 4 capacitors.

Claim 85 (original): The apparatus of claim 68 comprising permanent magnetic elements located within the second coil.

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Claim 86 (original): The apparatus of claim 85 wherein the permanent magnetic elements locally increase the strength of the magnetic field within the second coil.

Claim 87 (original): The apparatus of claim 67 wherein the fields are of a strength of at least 0.7 Tesla.

Claim 88 (original): The apparatus of claim 67 wherein the magnetic field is of a strength of about 1.5 to about 2.0 Tesla.

Claim 89 (original): The apparatus of claim 67 wherein the magnetic field is of a strength of at least 3.0 Tesla.

Claim 90 (original): The apparatus of claim 67 wherein the fields vary at a period of about once every two minutes.

Claim 91 (original): The apparatus of claim 67 wherein the period at which the magnetic field is activated and deactivated is from about 0.5 to about 10 seconds per pulse.

Claim 92 (original): The apparatus of claim 67 wherein the period at which the magnetic field is activated and deactivated is from about 1.0 to about 2.0 seconds per pulse.

Claim 93 (original): The apparatus of claim 67 wherein the period at which the magnetic field is activated and deactivated is about 2.0 seconds per pulse.